PharmaForce, Inc.

March 25, 2002

Dockets Management Branch
Food and Drug Administration (HFA-305)
5630 Fishers Lane
Room 1061
Rockville, MD 20852

CITIZEN PETITION

Dear Sir or Madam:

This petition is submitted in quadruplicate pursuant to 21 CFR 10.30 and in accordance with the regulations of 21 CFR 314.161, requesting the Commissioner of the Food and Drug Administration to provide a determination whether a listed drug has been voluntarily withdrawn for safety or effectiveness reasons, as outlined below.

A. Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration determine whether Phenergan® (Promethazine Hydrochloride Injection USP) 25 mg/mL, 10-mL, (NDA No. 08-857), by Wyeth Laboratories Inc., a Wyeth-Ayerst Company, has been voluntarily withdrawn or withheld from sale for safety or efficacy reasons.

B. Statement of Grounds

The publication, *Approved Drug Products with Therapeutic Equivalence Evaluations* (the List / Orange Book), identifies drug products approved on the basis of safety and effectiveness by the Food and Drug Administration (FDA) under the Federal Food, Drug, and Cosmetic Act (the Act). The main criterion for the inclusion of any product is that the product is the subject of an application with an effective approval that has not been withdrawn for safety or efficacy reasons.

Please note, the current edition of the "Electronic Orange Book" (*Approved Drug Products with Therapeutic Equivalence Evaluations)* lists Phenergan® (Promethazine Hydrochloride Injection USP) 25 mg/mL, Product 002 (1 mL), (NDA No. 08-857), by Wyeth Laboratories Inc., a Wyeth-Ayerst Company, in the Drug Product List section. Although not currently marketed, the drug product was also available in a 10-mL multidose configuration, as evidenced by its inclusion in the 1973 Physician's Desk Reference (see attached). Both the 10-mL and 1-mL configurations have the same product formulation. The 10-mL configuration is not listed in either the Drug Product List or Discontinued Drug Product List sections of the Orange Book.

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02P-0127

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As of the date of this submission, Phenergan® (Promethazine Hydrochloride Injection USP) 25 mg/mL, 10-mL, (NDA No. 08-857), by Wyeth Laboratories Inc., a Wyeth-Ayerst Company, is not available in the marketplace. Because there is no current commercial distribution of this drug product, it is requested that the Food and Drug Administration determine whether Wyeth's decision not to market Phenergan® (Promethazine Hydrochloride Injection USP) 25 mg/mL, 10-mL, was for reasons of safety or effectiveness.

C. Environmental Impact

A claim for categorical exclusion of the requirements for an environmental assessment is made pursuant to 21 CFR 25.31.

D. Economic Impact

Pursuant to 21 CFR 10.30(b), economic impact information is submitted only when requested by the Commissioner. This information will be promptly provided, if so requested.

E. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that includes representative data and information known to the petitioner, which are unfavorable to the petition.

Sincerely,

Marilyn A. Friedly
Director
Regulatory Affairs

PDR

27 EDITION

1973

Physicians' Desk Reference®

To Pharmaceutical Specialties and Biologicals

Publisher: CHARLES E. BAKER, Jr.
Production Manager: GEORGE E. QUIST, Jr.
Compilation Editor: BARBARA B. HUFF
Medical Consultant: AUSTIN JOYNER, M.D.
Ass't To Production Manager: BETTY CARUSO
Editorial Assistants: EMILY BROGELER, JAN CLARK, F. EDYTHE PATERNITI, DIANE M. WARD
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Fulfillment Manager: WILLIAM R. BOBBINK

PHENERGAN®

(promethazine hydrochloride)

INJECTION

Description: Each cc. of injection contains either 25 mg. or 50 mg. promethazine hydrochloride with 0.1 mg. disodium edetate, 0.04 mg. calcium chloride and not more than 0.25 mg. sodium metabisulfite and 5 mg. phenol with sodium acetate buffer.

Indications: The injectable form of promethazine hydrochloride is indicated for the following conditions when use of the oral form is impractical:

Amelioration and prevention of allergic reactions to blood or plasma in patients with a known history of such reactions.

In anaphylaxis as an adjunct to epinephrine and other standard measures after the acute symptoms have been controlled.

For other uncomplicated allergic conditions of the immediate type when oral therapy is impossible or contraindicated.

Active treatment of motion sickness.

Preoperative, postoperative and obstetric (during labor) sedation.

Prevention and control of nausea and vomiting associated with certain types of anesthesia and surgery.

As an adjunct to analgesics for the control of postoperative pain.

For sedation and relief of apprehension and to produce light sleep from which the patient can be easily aroused.

Intravenously in special surgical situations, such as repeated bronchoscopy, ophthalmic surgery, and poor risk patients, with reduced amounts of meperidine as an adjunct to anesthesia and analgesia.

Contraindications: Phenergan is contraindicated in individuals with a known hypersensitivity to the drug.

The intraarterial injection of promethazine hydrochloride is contraindicated.

Warnings: The sedative action of promethazine hydrochloride is additive to the sedative effects of central nervous system depressants; therefore, agents such as alcohol, barbiturates and narcotic analgesics should either be eliminated or given in reduced dosage in the presence of promethazine hydrochloride. When given concomitantly with promethazine hydrochloride the dose of barbiturates should be reduced by at least one-half and the dose of analgesic depressants, such as morphine or meperidine, should be reduced by one-quarter to one-half.

Although the proper intravenous use of promethazine is well-tolerated, care should be exercised not to allow perivascular extravasation since under such circumstances chemical irritation may occur.

When used intravenously, promethazine hydrochloride should be given in a concentration no greater than 25 mg. per cc. and at a rate not to exceed 25 mg. per minute (See note under Dosage and Administration).

Precautions: Ambulatory patients should be cautioned against driving automobiles or operating dangerous machinery until it is known that they do not become drowsy or dizzy from promethazine hydrochloride therapy.

Antiemetics may mask the symptoms of an unrecognized disease and thereby interfere with diagnosis.

Patients in pain who have received inadequate or no analgesia have been noted to develop "athetoid-like" movements of the upper extremities following the parenteral administration of promethazine. These symptoms usually disappear upon adequate control of the pain.

Adverse Reactions: Patients may occasionally complain of autonomic reactions such as dryness of the mouth, blurring of vision and, rarely, dizziness.

Very rare cases have been reported where patients receiving promethazine have developed leukopenia. In one instance agranulocytosis has been reported. In nearly every instance reported other toxic agents known to have caused these conditions have been associated with the administration of promethazine.

Cardiovascular by-effects from promethazine have been rare. Minor increases in blood pressure and occasional mild hypotension have been reported.

Photosensitivity, although extremely rare, has been reported. Occurrence of photosensitivity may be a contraindication to further

treatment with promethazine or related drugs.

Attempted suicides with promethazine have resulted in deep sedation, coma, rarely convulsions and cardiorespiratory symptoms compatible with the depth of sedation present. A paradoxical reaction has been reported in children receiving large single doses, characterized by hyperexcitability and nightmares.

Dosage and Administration:

Note: When using vials of parenteral Phenergan (promethazine HCl) following inital puncture of the closure, store preferably in the refrigerator. When used intravenously, it should be given in a concentration no greater than 25 mg. per cc. The rate of intravenous administration should not exceed 25 mg. per minute.

Allergy: When the oral route is not feasible Phenergan given intramuscularly or intravenously may be used. The average dose is 25 mg. The dose may be repeated within two hours if necessary, but oral therapy should be resumed if indicated and existing circumstances permit.

Children tolerate promethazine hydrochloride well. Single 25 mg. doses at bedtime or 6.25 to 12.5 mg. taken three times daily will usually suffice. After initiation of treatment in children or adults, dosage should be adjusted to the smallest amount adequate to relieve symptoms.

The administration of promethazine hydrochloride in 25 mg. doses prior to or during blood transfusion will prevent or control minor transfusion reactions of an allergic nature.

Motion Sickness: The average adult dose for the active treatment of motion sickness is 25 mg. When oral medication cannot be tolerated, the dose should be given intravenously or intramuscularly. 12.5 to 25 mg. doses may be repeated as necessary at four to six hour intervals.

Nausea and Vomiting: The average effective dose of Phenergan for the active therapy of nausea and vomiting associated with certain types of anesthesia and surgery is 25 mg. When oral medication cannot be tolerated, the dose should be given intravenously or intramuscularly. 12.5 to 25 mg. doses may be repeated as necessary at four to six hour intervals.

For prophylaxis of nausea and vomiting, as during surgery and the postoperative period, the average dose is 25 mg. repeated at four to six hour intervals as necessary.

For nausea and vomiting in children the dose should be adjusted to the age and weight of the patient and the severity of the condition being treated.

Sedation: This product relieves apprehension and induces a quiet sleep from which the patient can be easily aroused. Administration of 12.5 to 25 mg. Phenergan at bedtime will provide sedation in children. Adults usually require 25 to 50 mg. for nighttime, presurgical or obstetrical sedation.

Pre and Post Operative Use: Phenergan in 12.5 to 25 mg. doses for children and 50 mg. doses for adults the night before surgery relieves apprehension and produces a quiet sleep.

For preoperative medication, children require doses of 0.5 mg. per pound of body weight in combination with an equal dose of meperidine and the appropriate dose of an atropine-like drug. Usual adult dosage is 50 mg. Phenergan with an equal amount of meperidine and the required amount of a belladonna alkaloid.

For postoperative sedation and adjunctive use with analgesics, the dose is 12.5 to 25 mg. in children and 25 to 50 mg. in adults.

Obstetrics: Phenergan in doses of 50 mg. will provide sedation and relieve apprehension in the early stages of labor. When labor is definitely established, administer 25 to 75 mg. (average dose 50 mg.) promethazine hydrochloride intramuscularly or intravenously with 25 to 75 mg. meperidine (average dose 50 mg.). Amnesic agents may be administered as necessary. If the average doses of Phenergan and meperidine are used, it is seldom necessary to repeat the medication during a normal labor. If necessary, 25 to 50 mg. doses, with or without a reduced dose of analgesic, may be repeated once or twice, at three to four hour intervals.

How Supplied: Phenergan® Injection (promethazine hydrochloride) for IM or IV use, 25 mg. per cc.-ampuls of 1 cc., packages of 25; vials of 10 cc.; for IM use only, 50 mg. per cc.-ampuls of 1 cc., packages of 25; vials of 10 cc.

From: MARILYN FRIEDLY (614)486-7360
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COLUMBUS, OH, 43212

REVENUE BARCODE

FedEx.

To: Dockets Management Branch (301)594-0340
Food and Drug Admin. HFD-305
5630 Fishers Lane
Room 1061
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